

### **REMARKS**

Applicant respectfully requests reconsideration. Claims 1-5, 8-20, and 27-41 were previously pending in this application. Claims 1 and 13 have been amended to clarify that the cellulose acetate or nitrocellulose filter having a pore size capable of retaining detergent- or urea-insoluble amyloid-like fibrils or amyloid protein aggregates. Support for the amendments can be found in the specification as filed at least at page 11, third full paragraph (under Figure 3) and page 12, third full paragraph (under Figure 6), and at page 19, first full paragraph, lines 2-5. As a result, claims 1-5, 8-20, and 27-41 are pending for examination with claims 1 and 13 being independent claims. No new matter has been added.

#### **Rejections under 35 U.S.C. § 112, first paragraph**

The Examiner rejected claims 1-5, 8-20, and 27-41 under 35 U.S.C. § 112, first paragraph as lacking enablement.

The Examiner indicated at page 3 of the Office Action mailed December 12, 2007 that the specification, "while being enabled for a method of detecting detergent-or urea-insoluble amyloid-like fibrils or amyloid protein aggregates using cellulose acetate or nitrocellulose filters having a pore size capable of retaining detergent- or urea-insoluble amyloid-like fibrils or amyloid protein aggregates, does not reasonably provide enablement for a method of detecting detergent-or urea-insoluble amyloid-like fibrils or amyloid-like fibrils or amyloid protein aggregates using any given cellulose acetate membrane or nitrocellulose filters." Claims 1 and 13 have been amended to clarify that the method includes using cellulose acetate or nitrocellulose filters having a pore size capable of retaining detergent- or urea-insoluble amyloid-like fibrils or amyloid protein aggregates, which is subject matter the Examiner indicates is enabled by the specification as filed.

Accordingly, withdrawal of the rejection of claims 1-5, 8-20, and 27-41 under 35 U.S.C. § 112, first paragraph is respectfully requested.

#### **Rejections Under 35 U.S.C. § 103**

The Examiner rejected claims 1-5, 8-12, 17-20, and 27-30 under 35 U.S.C. § 103(a) as being unpatentable over Notario et al. Archivio per le scienze mediche, 135(1): 1-8 (1978 Jan-Mar)

Abstract in view of Tanzi et al., US Patent No. 6,365,414. Applicant respectfully traverses the rejection.

To support a *prima facie* case for obviousness, the Examiner must demonstrate motivation to combine the teachings in the references to make the claimed invention, a reasonable likelihood of success in making the combination of references, and that the references teach every element of the claimed invention. Applicant submits that these requirements for a *prima facie* case of obviousness have not been met.

Applicant submits that the modification of Notario et al. in view of Tanzi et al. does not result in the instant invention and that the teaching of the references cannot be combined to make the invention as claimed. Notario et al., the primary reference relied upon by the Examiner, teaches use of cellulose acetate in electrophoretic protein separation. Tanzi et al. describes use of cellulose acetate to filter proteins. The Notario et al. reference teaches a use of a cellulose acetate membrane and a manner of using a cellulose acetate membrane that are both unrelated to the use or manner of using cellulose acetate membranes in the Tanzi et al. reference.

The Examiner states at page 7 of the Office Action mailed December 12, 2007 that “Notario taught that nitrocellulose membranes have inherent capacity to capture large sized protein molecules from biological samples including those subjected to urea- or detergent-treatment for solubilization”. This conclusion is not supported by the Notario et al. abstract. As indicated by the Examiner at page 6 of the Office Action, “Notario is silent in teaching that the cellulose acetate membrane functions as a filter.” Notario et al. does not teach or suggest that a nitrocellulose membrane can be used to capture proteins but rather teaches that soluble proteins applied to a nitrocellulose membrane will move horizontally along the membrane upon application of an electrical current. The electrophoretic function described in Notario et al. is not a protein-capturing function. The electrophoretic separation of soluble proteins on a membrane as taught by Notario et al., is not a function that can be modified by the teaching of Tanzi et al. to capture insoluble proteins via a filtration method as in the instantly claimed invention.

The manner of using cellulose acetate membrane for electrophoretic separation as taught in the primary reference, Notario et al., cannot be modified in light of the filtration methods of Tanzi et al. to make the instant invention, without significant changes in the method of operation of the

cellulose acetate membrane method taught in Notario et al. As stated in the MPEP “if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.” MPEP 2143.01(VI) citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Thus, the combination of the teaching of Notario et al. with that of Tanzi et al. is not a proper basis for the rejection.

Although electrophoresis and filtration can each be performed with a cellulose acetate membrane, the manner in which a membrane is used in electrophoresis and the manner of its use in filtration are very different. In electrophoresis, a sample is applied at one end of a membrane, and due to an applied electric current, protein components of the sample are separated from each other as they migrate longitudinally along the membrane. The electrophoresed sample does not pass through the membrane but remains in the membrane and the sample components are separated along the membrane by the current – resulting in a pattern of proteins along the membrane. The purpose of the electrophoretic separation on the cellulose acetate membrane is to separate individual protein components on the basis of their electrical charge and to permit detection of the resulting longitudinal pattern of separated sample proteins on the membrane. In contrast, in filtration a sample is applied to a top surface of a membrane and components of the sample that are not retained by the membrane are washed or sucked from the top surface, through the membrane, and out through the bottom surface of the membrane. Unlike the electrophoretic separation method, no electric current is applied and there is no separation of proteins in the sample along the membrane and no resulting longitudinal pattern of separated proteins.

The use of cellulose acetate as an electrophoretic membrane material as taught by Notario et al. could not be modified by the teaching of Tanzi et al. to make the instant filtration-requiring invention without significant changes in the manner in which cellulose acetate membrane of Notario et al. is used. Modification of the teaching of Notario et al. to make the instant invention would change the operation of the cellulose acetate membrane from an electrophoretic surface to a filter that separates urea-soluble from urea-insoluble proteins, which is a significant, and patentably distinct, difference. The necessary modifications would “require a substantial reconstruction and redesign of the elements shown in [primary reference] as well as a change in the basic principles

under which the [primary reference] construction was designed to operate.” *In re Ratti*, at 813, USPQ at 352. Thus, the combination of Notario et al. in view of Tanzi et al. does not provide a basis for a *prima facie* case for obviousness.

In addition, the Examiner has not indicated specific motivation for one skilled in the art to combine the electrophoretic methods of Notario et al. with the teaching of Tanzi et al. to make the instantly claimed invention. As stated in the MPEP, “If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.” MPEP 2143.01(VI), citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Modification of the electrophoretic use of cellulose acetate disclosed in Notario et al. to a filtration use of cellulose acetate of the instant invention, would make the modified Notario et al. method unsatisfactory for its intended purpose.

Notario’s purpose for using a cellulose acetate membrane electrophoresis is to separate individual proteins of a sample from each other along the membrane – e.g., to generate an electrophoretic pattern of the sample proteins along the membrane, thus allowing identification of the sample proteins based on their migration pattern. Use of a filtration method of the instant invention to separate proteins in a sample separates urea-insoluble from urea-soluble proteins, but does not separate sample proteins from each into a separation pattern along a membrane. The cellulose acetate electrophoretic method of Notario et al., modified as suggested by the Examiner, would not be suitable for its intended purpose as set forth in the Notario et al. abstract. Thus, there is no motivation to combine the references in the manner suggested by the Examiner to modify the teaching of Notario et al. to make the claimed invention.

Accordingly, withdrawal of the rejection of claims 1-5, 8-12, 17-20, and 27-30 under 35 U.S.C. § 103(a) as being unpatentable over Notario et al. *Archivio per le scienze mediche*, 135(1): 1-8 (1978 Jan-Mar) Abstract in view of Tanzi et al., US Patent No. 6,365,414 is respectfully requested.

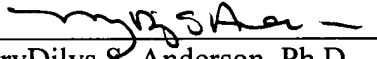
**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

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Respectfully submitted,

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